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【 CASE REPORT 】

Secondary Cardiac Lymphoma Presenting as Sick Sinus Syndrome and Atrial Fibrillation Which Required Leadless Pacemaker Implantation

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Abstract:
Cardiac involvement of malignant lymphoma is relatively common, although such a phenomenon has subclinical manifestations that are difficult to detect. We herein describe a patient with atrial fibrillation and sick sinus syndrome as the main symptoms. Computed tomography showed a mass in the right atrium extending into the superior vena cava (SVC). We implanted the patient with a leadless pacemaker. Transvenous biopsy revealed a diffuse large B-cell lymphoma. The patient was treated successfully with chemotherapy including rituximab. This case suggested that cardiac lymphoma may cause sick sinus syndrome, and leadless pacemaker implantation is a safe treatment option in patients with partial SVC obstruction.

Key words: cardiac lymphoma, sick sinus syndrome, atrial fibrillation, leadless pacemaker

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Introduction

Secondary cardiac involvement of lymphoma is relatively common, reported in 8.7-25% of documented clinical cases of lymphoma (1). Nevertheless, manifestations of cardiac involvement of lymphoma are often subclinical, thus, cardiac involvement as an initial presentation of malignant lymphoma is rare (2, 3).

We herein present a patient with syncope and palpitation as the main symptom of malignant lymphoma with cardiac involvement. The patient was treated successfully with chemotherapy and the implantation of a leadless pacemaker.

Case Report

An 85-year-old man with recent history of syncope and palpitations was admitted to our medical center. His medical history included dyslipidemia and prostatic hypertrophy. On physical examination, he had a low-grade fever and an irregular heartbeat. There was no superficial lymphadenopathy. The electrocardiogram (ECG) at presentation showed atrial fibrillation and frequent sinus pauses (Fig. 1A). Laboratory tests showed elevated levels of lactate dehydrogenase 1,085 U/L, C-reactive protein 17.2 mg/dL, and B-type natriuretic peptide 453.7 pg/dL levels. A transthoracic echocardiogram revealed pericardial effusion with normal contraction. Computed tomography (CT) showed mediastinal lymphadenopathy and a mass in the right atrium extending into the superior vena cava (SVC) and left atrium (Fig. 2A, B). The ensuing transesophageal echocardiogram showed the presence of a mass arising from the mediastinum and protruding into both atria. Magnetic resonance imaging (MRI) showed a tumor in the right atrium partially obstructing the SVC. For a definitive diagnosis, transvenous biopsy of the cardiac mass was undertaken under angiography guidance. Because of the partial SVC obstruction, the risk of pulmonary tumor embolism, and the difficulty of transvenous

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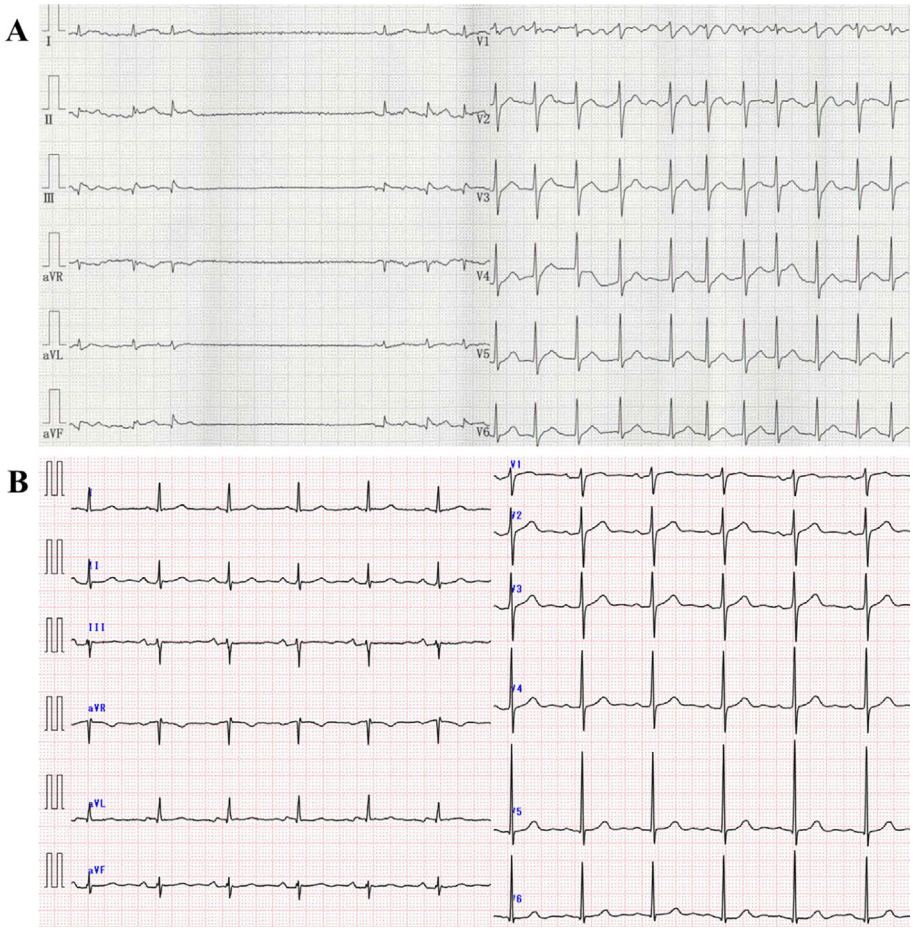

Figure 1. **A: Electrocardiogram (ECG) results on admission showing atrial fibrillation with sinus arrest. B: ECG after eight cycles of chemotherapy showing normal sinus rhythm.**

pacemaker insertion, a leadless pacemaker (Micra: Medtronic, Minneapolis, USA) was transfemorally inserted into the right ventricular cavity.

A pathologic examination of the cardiac mass revealed it to be a diffuse large B-cell lymphoma (immunohistochemical analysis: CD3-negative, CD20-positive, BCL2-positive, and Ki67 expression was 70%). A bone marrow biopsy did not show any evidence of lymphoma. The patient was diagnosed with stage II primary mediastinal large B-cell lymphoma according to the Ann Arbor Classification.

After eight cycles of chemotherapy with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone (R-CHOP), CT showed a marked reduction in the tumor mass size (Fig. 2C, D), and the ECG showed normal sinus rhythm (Fig. 1B). Further, pacemaker interrogation at 6-month follow-up revealed 0.4% ventricular pacing burden without atrial fibrillation. The patient's symptoms of syncope and palpitations thereafter also resolved.

Discussion

Secondary cardiac involvement of lymphoma

Cardiac tumors can be classified into primary cardiac tumors originating in the heart and secondary cardiac tumors metastasizing to the heart from other locations in the body. Primary cardiac lymphoma is a very rare tumor that is confined to the heart and pericardium and accounts for 1.3% to 3% of all primary cardiac tumors (4). In contrast, secondary metastatic involvement of the heart from extra cardiac tumors is 20-40 times more common than primary cardiac tumors (4), and secondary cardiac involvement of lymphoma is found in 8.7-25% of documented clinical cases of lymphoma (1).

Clinical aspects and diagnosis

The clinical presentations of cardiac involvement of lymphoma have relied on tumor location, size, growth speed, degree of invasion, and friability. These presentations might include arrhythmias, pericardial effusion or tamponade, tumor embolization and obstruction of blood flow, and valvular dysfunction. Arrhythmias caused by cardiac involvement of lymphoma include atrial flutter, atrial fibrillation, atrioventricular conduction disturbances, and sick sinus syndrome (5). The presentation of sick sinus syndrome is a rare occurrence in comparison to atrioventricular conduction disturbances (5). Although sick sinus syndrome is mostly caused by degenerative fibrosis of the sinus node associated with aging, infiltration of leukemia or cancer, amyloidosis, fatty replacement, arteritis, and myocarditis have been re-

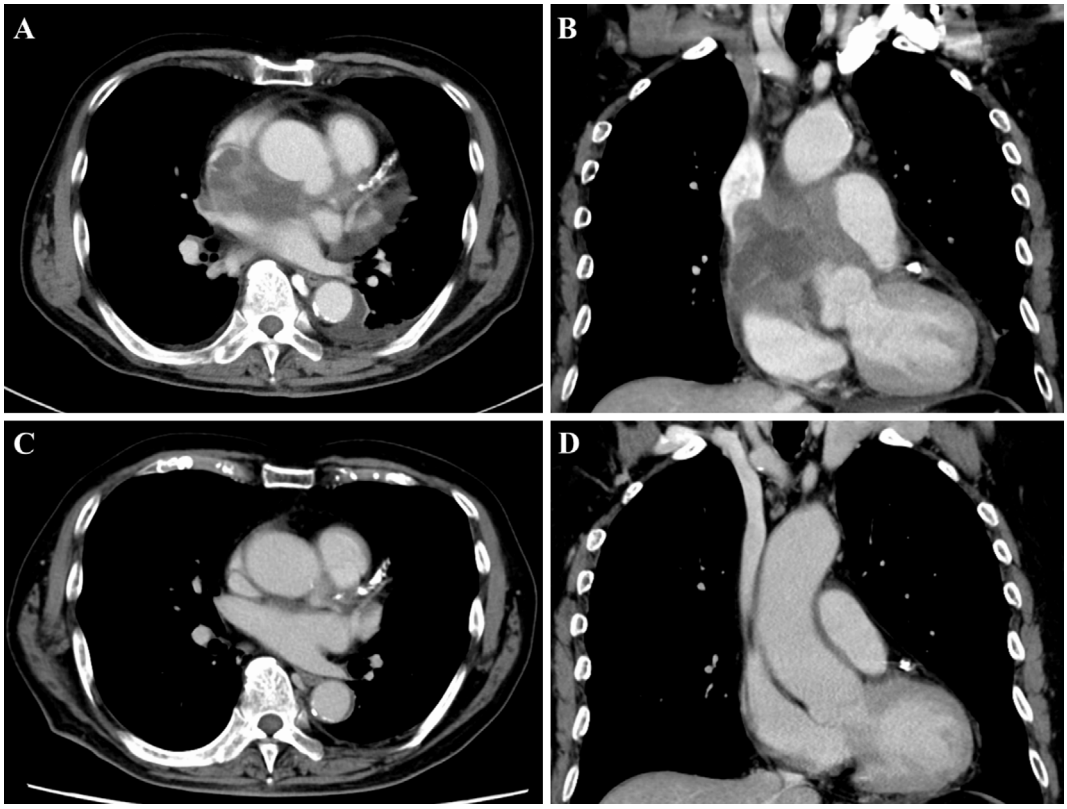

Figure 2. **A, B: Computed tomography (CT) demonstrating the mass in the right atrium prolapsing into the superior vena cava (SVC) and left atrium. C, D: CT after eight cycles of chemotherapy demonstrating a marked reduction in the tumor mass size.**

ported as the cause of sick sinus syndrome as well (6). Therefore, the possibility of cardiac involvement of lymphoma should be acknowledged in patients presenting with sick sinus syndrome with unknown causes (6). The cardiac involvement of lymphoma is often subclinical (7, 8), therefore cardiac involvement as an initial presentation of malignant lymphoma is rare (9). Our patient initially presented with syncope and palpitation, and his ECG showed atrial fibrillation and sick sinus syndrome. As a result, he was diagnosed with secondary cardiac lymphoma.

Echocardiogram is the initial noninvasive screening modality for examining the heart and pericardium. However, transesophageal echocardiogram providing a larger imaging field has better sensitivity for the detection of cardiac involvement of lymphoma (10). CT and MRI may help determine morphology, location, extension of tumor, and blood flow (2).

A tumor biopsy is essential in the diagnosis of lymphoma. Though direct thoracotomy has been conventionally performed, less invasive procedures have recently been carried out. These include transesophageal echocardiography-guided biopsy, transvenous angiography-guided biopsy, mediastinoscopic biopsy, and thoracoscopic biopsy (2). In case of pericardial effusion, cytological examination is useful to prevent the risk of embolism through direct biopsy (11).

Treatment and prognosis

The prognosis of cardiac involvement of lymphoma is usually poor due to diagnostic delay. The treatment most commonly includes chemotherapy; occasionally, radiation therapy and surgery are combined with chemotherapy (12). The main chemotherapy regimen for cardiac lymphoma has been CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone). Currently, the addition of monoclonal CD 20 antibody (rituximab) to the CHOP regimen has led to a good response and an increased overall survival rate in CD 20-positive patients (12).

Leadless pacemaker implantation

When cardiac involvement of lymphoma occurs, the right atrium is most commonly affected, with subsequent venous extension leading to partial SVC occlusion, as in our case (12). In addition to the risk of pulmonary tumor embolism during dual-chamber pacemaker insertion (13), manipulation of the transvenous lead by passing through the partially occluded SVC seemed challenging. Although epicardial pacemaker implantation has been reported as an alternative treatment for sick sinus syndrome or atrioventricular conduction disturbances caused by cardiac lymphoma (5, 14), the procedure is highly invasive. Leadless pacemaker is a capsule-shaped device with a small battery possessing surface electrodes capable of endocardial sensing and pacing, and can be implanted non-surgically via the femoral vein. As there is no transvenous lead and no subcutaneous pocket, it is possible to avoid the many potential adverse events associated with these components (15, 16). In

patients with sick sinus syndrome, ventricular pacing increases the risk of atrial fibrillation, as compared with dual-chamber pacing (17). However, recovery of the sinus function and reduction of ventricular pacing requirements can be expected, when the lymphoma is highly sensitive to chemotherapy (18).

In our case, a patient presented with symptomatic sick sinus syndrome and was successfully treated by the implantation of a leadless pacemaker. To the best of our knowledge, there have been no reported cases of leadless pacemaker implantations for sick sinus syndrome in patients with partial SVC obstruction due to secondary cardiac lymphoma. The choice of leadless pacemaker implantation can reduce the risk of pulmonary tumor embolism as well as minimize the risk of infection and hematoma associated with the expected pancytopenia following chemotherapy (18).

Conclusion

Although uncommon, the diagnosis of cardiac lymphoma should be considered in patients presenting with arrhythmias such as sick sinus syndrome and atrial fibrillation. Additionally, leadless pacemaker implantation can be a useful choice of treatment for symptomatic bradycardia and partial SVC obstruction in such patients.

The authors state that they have no Conflict of Interest (COI).

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